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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/652,864	08/29/2003	Heinz Kohler	200-019	1487

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EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
11/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/652,864	KOHLER ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6* is/are rejected.

7)☒ Claim(s) *7-10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The applicant has timely traversed the non-final rejection in the reply filed on 09/14/2007, and a response to the arguments is set forth.

2. Claims 6-10 are under examination.

Rejections Withdrawn

3. The rejection of claim 6 rejected under 35 U.S.C. 102(a) as being anticipated by Zhao[a] et al (J. Immunotherapy. 2002, 25:57-62; IDS – 11/07/2005) is withdrawn in view of the declaration submitted by the applicant.

4. The rejection of claims 6-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao[a] et al (J. Immunotherapy. 2002, 25:57-62; IDS – 11/07/2005) in view of Kohler et al (U.S Patent 6238667, Date Issued: May 29th, 2001) and Zhao[b] et al (J. Immunol. Methods. 2001. 254:137-145; IDS – 11/07/2005), Singh et al (U.S. Patent 7041459; Date Filed: May 21st 2002) and Rojas et al (Nature Biotechnology, 1998. 16:370-375) is withdrawn in view of the declaration submitted by the applicant.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 recites the limitation "the immunoglobulin component" in lines 3-4 of the claim. There is insufficient antecedent basis for this limitation in the claim.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing an autophilic antibody by a chemical or genetic engineering techniques, wherein the autophilic antibody contains a T15 autophilic peptide having an amino acid sequence shown in SEQ ID NO:1 photo-crosslinked to a heterocycle or nucleotide affinity site of the immunoglobulin or crosslinked to a carbohydrate site of the Fc portion or to an amino or sulfhydryl group of the immunoglobulin, in addition to being expressed as a fusion protein of the T15 peptide and whole immunoglobulin, or fragment thereof, does not reasonably provide enablement for a method of producing an autophilic antibody by a chemical or genetic engineering techniques, wherein the autophilic antibody contains a T15 autophilic peptide having an amino acid sequence shown in SEQ ID NO:1 attached to <u>any</u> immunoglobulin component of the antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention is engineering autophilic antibodies where the relative level of skill of those in the art is deemed to be high.

The claim is drawn to a method of producing an autophilic antibody by a chemical or genetic engineering techniques, wherein the autophilic antibody contains a T15 autophilic peptide having an amino acid sequence shown in SEQ ID NO:1 attached to "the immunoglobulin component" of the antibody. Thus, the claim is broadly drawn to an autophilic antibody wherein the autophilic peptide is attached to any site of the immunoglobulin component of the antibody. The immunoglobulin component, by definition, includes any part of the antibody including the variable regions, constant regions and the hinge regions. Thus, the claim is drawn to an autophilic antibody wherein the autophilic peptide is attached to any site of the immunoglobulin molecule, without specifying the particular site of the immunoglobulin, which may not necessarily have the structure and function of an autophilic antibody, be definition.

The specification discloses (paragraph 20, in particular) that the T15 peptide can be photo-crosslinked to a heterocycle or nucleotide affinity site of the immunoglobulin to produce the autophilic antibody. Alternatively, the T15 peptide can be crosslinked to a carbohydrate site of the Fc portion or to an amino or sulfhydryl group of the immunoglobulin. Also, the autophilic antibody can be conveniently expressed as a fusion protein of the T15 peptide and whole immunoglobulin, or fragment thereof.

It is well known in the art the art that the autophilic antibodies have a higher potential for forming dimers when conjugated to suitable peptides and can have a therapeutic potency through triggering apoptosis. Hence, maintaining such efficiency and high binding avidity of the antibody becomes important for determining the site where the autophilic antibody is to be attached. Kohler et al (U.S. Patent 6,238,667) teach (paragraph 4-12, in particular) that the hetero-bifunctional cross-linkers are used which cross-link the selected molecules at random sites on the immunoglobulin molecule. However, such hetero-bifunctional cross-linking is associated with two problems: first, the antibody structure is compromised by local protein denaturation at the sites of cross-linking, which leads to changes in half-life in blood and biodistribution and uptake by scavenger cells in lung and liver; second problem is the potential loss of antigen binding by non-specific cross-linking to the antigen binding site. Thus, the site of attachment has to be carefully selected in order to avoid compromising antigen binding and/or stability of the heavy-light chain dimer structure. Kohler et al further teach that the autophilic attachment site of the antibody is highly

conserved and consists of framework residues within the variable domain domains of the heavy and light chains of the antibody; in addition to that the site of cross-linking is located away from the antigen-binding site in the Fv domain, thereby avoiding compromise of antigen recognition.

The specification provides no direction or guidance regarding how to produce a method of producing an autophilic antibody by a chemical or genetic engineering techniques, wherein the autophilic antibody contains a T15 autophilic peptide having an amino acid sequence shown in SEQ ID NO:1 attached to any immunoglobulin component of the antibody as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone. The scope of the claims must bear a reasonable correlation with the scope of enablement. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

In view of the lack of the predictability of the art to which the invention pertains, the lack of guidance and direction provided by applicant, and the absence of working examples, undue experimentation would be required to practice the claimed autophilic antibody.

7. Claims 7-10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi
Ph: (571) 272-8789

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER